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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,112	12/31/2001	John J. Egan	361331-506	5381
30623 7590 10/18/2007 MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C. ONE FINANCIAL CENTER BOSTON, MA 02111			EXAMINER KWON, BRIAN YONG S	
			ART UNIT 1614	PAPER NUMBER
			MAIL DATE 10/18/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/038,112

Applicant(s)

EGAN ET AL.

Examiner

Brian S. Kwon

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 4, 8, 9, 11 and 13-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 8, 9, 11 and 13-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114. Claims 1, 2, 4, 8, 9, 11 and 13-17 are currently pending for prosecution on the merits.

2. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

#### ***Claim Objections***

3. Claims 1 and 8 are objected to because of the following informalities: There are more than one periods used in claims 1 and 8. See MPEP 608.01(m).

Each claims begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2, 4, 8, 9, 11, 13-14 and 16-17 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The present invention are drawn to a method of decreasing intraocular pressure or improving ocular accommodation in a patient comprising administering “cholinergic agent” with the compound of the formula I.

The specification discloses pilocarpine (known cholinergic agonist) as a suitable example of “cholinergic agent”, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, the claims are directed to encompass “cholinergic agent” which only correspond in some undefined way to specifically instantly disclosed chemicals, including not only cholinergic agonist but also cholinergic antagonist, mixed cholinergic agonist/antagonist and indirect cholinergic agonist or antagonist. None of these meet the written description provision of 35 USC 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompasses a myriad of possibilities. To the extent that no structure function data is disclosed in connection with these functionally described compounds to correlate, or there is not disclosed correlation established between these functional drugs and the contemplated desired therapeutic effect to be achieved in practicing the instant invention, the specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116).

With the exception of pilocarpine, the skilled artisan cannot envision “cholinergic agent”, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF’s were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”) Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 4, 8, 9, 11 and 13-17 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for “pilocarpine” with the combination of the specific compound of the formula I such as 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolidum chloride for decreasing intraocular pressure, does not reasonably provide enablement for use of “cholinergic agent” with the compound of the formula I for decreasing intraocular pressure or improving ocular accommodation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The present invention are drawn to a method of decreasing intraocular pressure or improving ocular accommodation in a patient comprising administering “cholinergic agent” with the compound of the formula I.

The interpretation of the instant claims allows for the inclusion of any known cholinergic agents having agonist, antagonist or mixed agonist/antagonist property that are known to exist and those that may be discovered in the future. Furthermore, the instant compounds represented by the formula embrace compounds with substituents bearing plethora of structural cores (e.g., Q is N, O or S) and functional groups and other groups which include variously substituted C5-C10 aryl ring or aromatic fused ring with variable ring sizes and variable heteroatoms variety of reactive functional groups. In other words, the breadth of the instant invention encompasses the combination of plethora of compounds represented by the formula I and various cholinergic agents that may have totally different activities depending upon their different affinity at cholinergic receptor site.

The specification discloses that the present invention relates to a method of decreasing the intraocular pressure caused by glaucoma and that the administration of the compound of the formula I, particularly 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolidum chloride, having property of inhibiting formation of the advanced glycsylation end product (AGE), in combination with pilocarpine (known cholinergic agonist), would be useful in the treatment of glaucoma by decreasing intraocular pressure (page 1, lines 6-10; page 12, lines 18-26; Figures and Table).

It is generally recognized in the art that biological compounds often react unpredictably under different circumstances (Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5<sup>th</sup> Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)). There is no reasonable basis for

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assuming that the myriad of compounds embraced by the claim language will all share the same bioactivity profile since they are so functionally different (as to "cholinergic agent") or structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same (as to "a compound of the formula I"). Note *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive art such as the pharmaceuticals. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method of use. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards utility in humans or animals, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims. Furthermore, representative examples of structurally diverse compounds generically embraced in the invention by reciting physiologically acceptable derivative are not shown to possess *in vitro* activity much less *in vivo* uses claimed herein.

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

The examiner acknowledges that the Office does not require the present of (all) working examples to be present in the disclosure of the invention (see MPEP 2164.02). However, given



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the highly unpredictable state of the art and furthermore, given that the applicant does not provide sufficient guidance or direction as to how to use the full scope of the presently claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of the elected species for the full scope of the presently claimed subject matter. Absent such evidence or reasoning, applicant has failed to obviate the rejection of the instant claims under 35 USC 112, first paragraph (for the lack of scope of enablement).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 2, 4, 8, 9, 11 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 1 recites "improving ocular accommodation". The specification does not define the term and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

### Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon  
**Primary Patent Examiner**  
**AU 1614**

A handwritten signature in black ink, appearing to be 'B. Kwon', with a long horizontal line extending to the right.